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IDENTIFICATION OF PRIORITY PHARMACEUTICAL RESIDUES IN HOSPITAL EFFLUENTS

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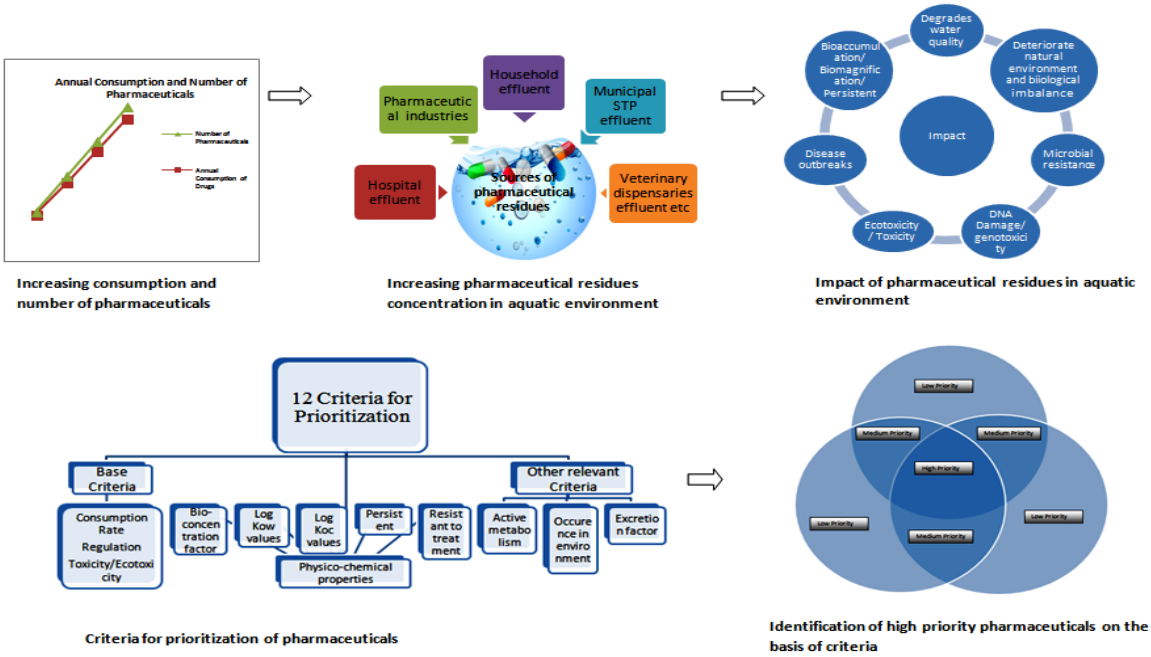
ABSTRACT

The pharmaceutical residues are commonly found in aquatic environment throughout the world. The pharmaceutical residue increases the microbial resistance, reduces the self purification capacities of the water bodies, adversely impacts the aquatic life being ecotoxic and few are also known to be teratogenic, mutagenic and even genotoxic. Despite of well documented and known potential implications of pharmaceutical residues, they persist in the aquatic environment and there are still no specific discharge standards. This study has attempted to consider extensive set of important parameters for identifying the pharmaceuticals that have worst impact on aquatic environment. The three priority lists comprising of the most commonly consumed pharmaceuticals have been developed; high priority list consists of 09 pharmaceuticals; moderate priority list includes 19 pharmaceuticals and low priority list with 6 pharmaceuticals. The high priority pharmaceuticals hold maximum importance from the point of view of aquatic environment and they should be analyzed in the effluent of hospitals and other sources before it is discharged into the water bodies. It can be regarded as first step for development of pharmaceutical residues standards and for managing the risks of pharmaceutical pollution.

GRAPHICAL ABSTRACT



Key words: *Pharmaceutical residues, priority pharmaceuticals, criteria for prioritization, water body, effluent, hospitals.*

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I. INTRODUCTION

Delhi, being the capital city of India is a major hub of health care facilities. There are around 48,000 beds in health care facilities of Delhi as per Delhi Pollution Control Committee. The number of beds and hospitals are increasing day by day to meet the growing demand for health care of local, national as well as international patients, thus leading to increased consumption in Delhi.

The effluent generated by hospitals is loaded with pathogenic microbes, incompletely metabolized radioactive substances, heavy metals, pharmaceutical residues, disinfectants, traces of blood, body fluids and other toxic substances (1). The effluents if discharged untreated/ partially treated can deteriorate the natural environment by degradation of water quality, deterioration of natural environment, microbial resistance, genotoxicity, ecotoxicity, disease outbreaks, bioaccumulation and persistence in aquatic environment. The hospital effluent requires treatment at the source to prevent contamination of the water bodies (2)(3).

If the pharmaceutical residues are not easily degraded or removed by the sewage treatment process then it reaches the aquatic environment and comes back in drinking water system. Many research studies have reported the pharmaceutical residues in surface water, ground water and even in potable water (4). The occurrence, metabolism and toxicity of pharmaceutical residues belonging to different therapeutic classes like Non-Steroidal anti-inflammatory pharmaceuticals (NSAIDs), antibiotics, beta-blockers, estrogens, lipid regulators, antiphlogistics, psychiatric pharmaceuticals, antiepileptic pharmaceuticals, cytostatic pharmaceuticals and antihistamines have been found in the aquatic environment including surface water, groundwater and potable water. (5)(6)

Some investigations have been carried out in different countries like Spain, Greece, England, Canada, Italy, Austria, Brazil, Croatia and USA, wherein more than 100 pharmaceutical pharmaceuticals and its metabolites have been found in the water bodies. (7)(8)(9)(10)(11)(12)(13)(14)(16)(17). Mutiyar reported the pharmaceutical residues specially that of antibiotics in the River Yamuna of Delhi (15).

Despite of its potential implications on environment, aquatic life, water quality, microbial resistance, health and society, there are no discharge standards for hospital effluents in India. The parameters set for Indian hospitals are pH, TSS, BOD, COD, O&G and Bio-assay test for fishes (16). These standards are same as that for other industrial effluents. Till date there are no discharge standards with respect to pharmaceutical residues in hospital effluent.

Thousands of chemicals including pharmaceuticals, chemicals, solvents etc are used in the hospitals. There is a dire need to rank these pharmaceuticals and identify the priority pharmaceuticals on the basis of risk they pose to the environment. The priority pharmaceuticals can be defined as those pharmaceutical residues and their metabolites which have worst impact on environment due to their bio-accumulation potential or other physico-chemical properties. The toxicity assessment experiments and ecotoxicological assays should be done for these pharmaceuticals.

The extensive monitoring programmes for active pharmaceutical substances at source of generation as well as water bodies should be carried out. Thus, this paper aims at developing a list of priority pharmaceuticals for which toxicity assessment studies, analytical studies should be carried out in future and also at identifying important parameters to select the relevant pharmaceutical compounds from the point of view of environment.

II. METHODOLOGY

Selection of criteria

The criteria for selection of priority pharmaceuticals were based on extensive literature review on different prioritization criteria. Out of the initially screened 20 criteria, the 12 criteria have been identified as relevant on the basis of logical and scientific grounds. Figure 1 explains the procedure for selection of the criteria. The criteria selected for evaluation have been treated as equally important and thus, no further prioritization of the criteria has been considered. The pharmaceuticals are however, selected on the basis of certain additional risk factors. The first

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step screening was done to cut down the list of pharmaceuticals taken from literature by considering the consumption of the pharmaceutical in the inpatient department of the hospitals. There are many existing pharmaceuticals prioritization method those have used consumption and/or discharge as the base criterion for selection of pharmaceuticals.(17)(18)(19)(20)(21)(22)(24). Few of these also included bioaccumulation potential as one of the criteria as it is a fundamental risk factor for aquatic life. (23).

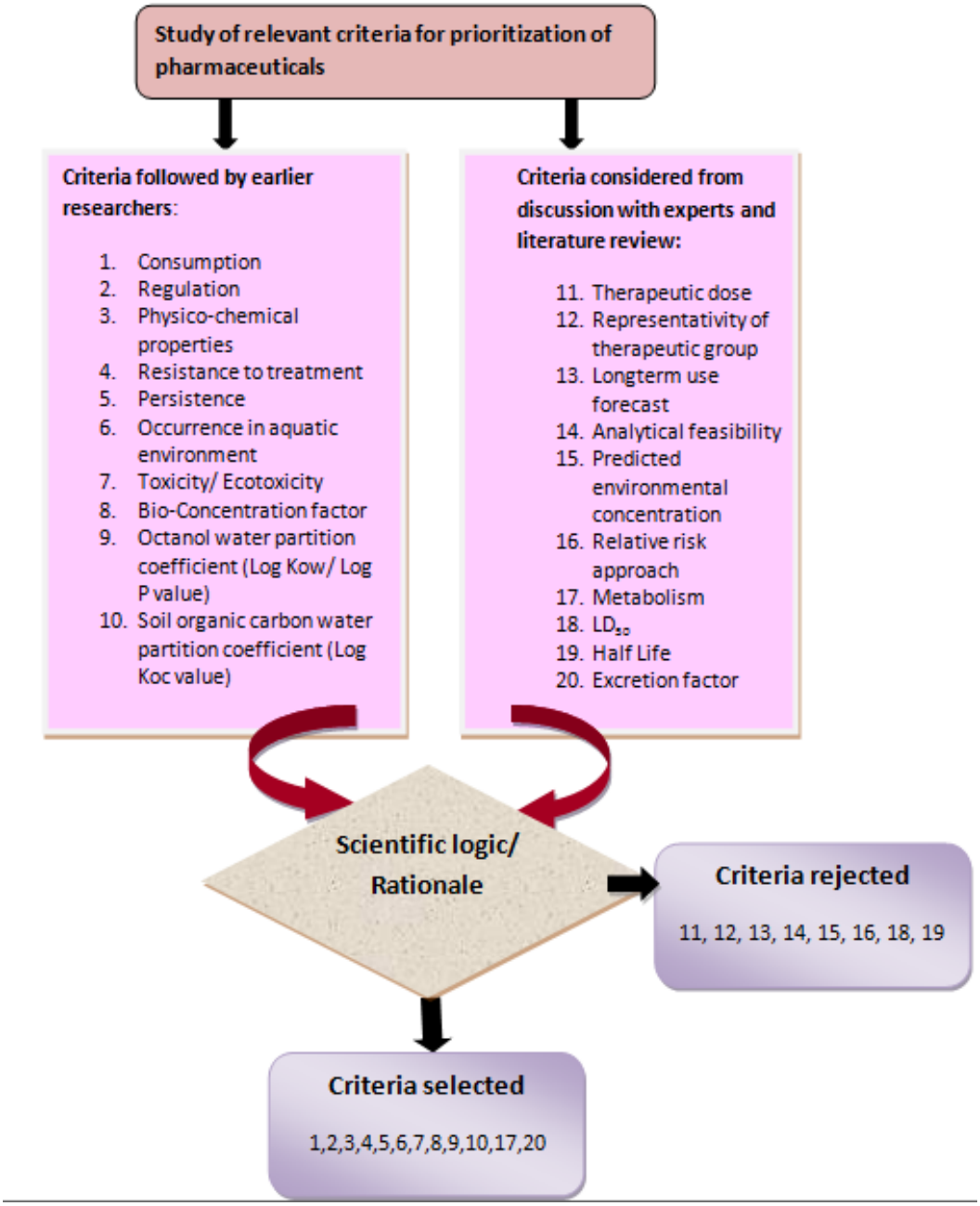

Figure 1: Flowchart showing selection of criteria

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III. PRIORITIZATION OF PHARMACEUTICALS AND RATIONALE FOR SELECTION OF CRITERIA

Through literature survey of the earlier prioritization studies, 20 criteria have been identified (24)(25)(26)(27). All the criteria have been given equal weightage. Accordingly, the 12 criteria have been finally selected for consideration. The 8 criteria have been rejected on logical grounds.

These 12 criteria can be used for prioritization locally as well as internationally. The selection of criteria is explained in the table 1.

Table 1 Selection of Criteria for prioritization

Criterion	Criterion selected	Rationale
Consumption	Yes	The consumption has been considered as the base criterion. Higher the consumption of the pharmaceutical, higher could be the concentration of pharmaceutical residues in the effluent. So, it has been taken as the base criterion for selection other than literature screening. The data of average monthly consumption of pharmaceuticals in inpatient department of 6 multi speciality hospitals of Delhi was collected. Also, annual consumption data was fetch from the Central Procurement Agency. Accordingly, pharmaceuticals have been selected for the study. (19)(20)(21)(22)(23)(24)(25)(26)
Regulation	Yes	The pharmaceuticals mentioned in any of the regulation across the world are relevant as they are listed only when they have relevant impact and its use is to be kept checked
Physico-chemical properties	Yes	The physico-chemical properties of a pharmaceutical decides its fate and behaviour in the aquatic environment eg its water solubility, sorption etc (23)(21)(27). These decide the relevance of a pharmaceutical residue in various compartments of aquatic environment.
Resistance to treatment	Yes	The pharmaceutical residues that are not easily removed by effluent treatment plants are definitely of high relevance (24)(20)(27). The data on persistence and removal of pharmaceuticals is minimal and needs to be developed in future. However, it is an important criterion for prioritization.
Occurrence in surface waters, groundwater, drinking water, wastewater	Yes	This is again a key criterion for selection because if the pharmaceutical residue is present in any compartment of aquatic environment, then there is a need to evaluate its relevance and behaviour (20)(21)(22)(27). The presence in wastewater is also considered important if it is present in influent as well as effluent.

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Bioconcentration factor	Yes	The bioaccumulation potential is estimated by the bio-concentration factor (25). The BCF explains the transfer of pharmaceutical residue from aquatic environment to living organism. This denotes the bio-accumulation potential of the pharmaceutical.
Log Kow value	Yes	This reflects the adsorption properties. It estimates molecular lipophilicity and it also predicts the accumulation potential. (20)(25)(26)
Excretion factor	Yes	This is an important criterion as it corresponds to the fraction of unchanged pharmaceutical excreted from the body through urine or faeces. This is important to assess the ecotoxicological risk. (25)(22)
Log Koc value	Yes	It refers to organic carbon partition coefficient that estimates the mobility of a pharmaceutical in soil. Low value indicates that it is mobile in soil and high values points towards its potential adverse effects on terrestrial organisms (25).
Persistent	Yes	The persistence can be understood by literature support and physicochemical properties. The pharmaceuticals that have been found to be persistent in aquatic system are important from the point of view of environment (27)(25).
Toxicity/ Ecotoxicity	Yes	It is the most important criterion to be considered. Since, it is a direct criterion that tells about the impact of pharmaceutical residues on aquatic life (27)(25). This is justified by the toxicity assessment studies done for the pharmaceuticals on various living organisms by researchers all over the world.
Metabolism	Yes	Although, the occurrence data can be considered as more relevant than this. But this can also be considered as one of the criteria for prioritization. Once a pharmaceutical is administered, it is degraded in the body and form metabolites. The metabolites excreted from the body can either be more active or less active. The active metabolites are also needed to be kept a check. Also, certain pharmaceuticals are excreted in high percentage as parent pharmaceutical. So, pharmaceutical consumption and metabolism/ excretion hand in hand can give a fair idea about the occurrence of pharmaceutical residue in ecosystem. However, even if a stable metabolite is formed, it may also be selected if it fulfils other criteria. This criterion was considered as per the expert's advice.
Therapeutic dose	No	The therapeutic dose is considered as a way of approaching predicted no effect concentration (27)(20). So, for this study, this does not seem to be relevant.

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Representativity of therapeutic group	No	Logically, there is neither a need nor it is feasible to study pharmaceuticals from each therapeutic group in the current scenario of lack of data availability on toxicity and fate of pharmaceuticals and their metabolites (27)(20). This criterion is not relevant to be a part of the selected criteria.
Long term use forecast	No	The current situation can't be evaluated by the long term use data (27)(24)(20). Also, most of the models for forecasting long term use exhibit irregularities and uncertainties. Therefore, it is not regarded as a good criterion.
Analytical feasibility	No	This is not considered as a relevant criterion for prioritization of pharmaceuticals. If a pharmaceutical is harmful to environment, there is a need to develop methods of detection and quantification (27). However, a pharmaceutical residue in the ecosystem can't be ignored if the method of analysis is yet to be developed.
Predicted environmental concentration	No	This criterion has not been included because the information can be revealed by consumption data and persistence. Although, the Predicted environmental concentration (PEC) values give a better idea of the situation (27).
Relative risk approach	No	This is calculated as ratio of predicted environmental concentration and predicted no effect concentration (PEC/PNEC). (27)(26)(22). This factor is not considered as it has already been covered under other criteria.
Half life	No	The pharmaceuticals having a half life of more than 48 hours are considered as accumulable in humans (25). However, this has not been considered as a principal criterion. The excretion factor and bio-concentration factor gives better idea of the environmental relevance of the pharmaceutical. This could be treated as an important criterion for clinical research but discarded for the prioritization of pharmaceutical from the environmental point of view.

Out of the 20 criteria mentioned above, following 12 criteria have been selected for prioritization. The criteria considered in this study are shown in Fig 2:

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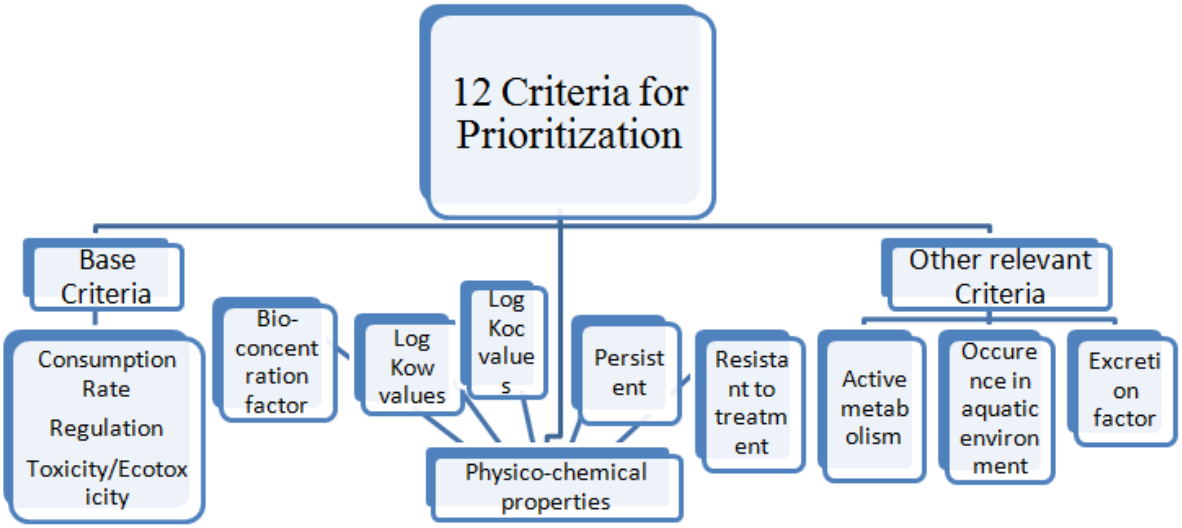

Figure 2 Criteria for prioritization

Pharmaceuticals selection

According to literature survey on prioritization of pharmaceutical residues, 86 pharmaceuticals were shortlisted from the literature for study. On the basis of ecotoxicity and toxicity; occurrence in water bodies around the globe and persistence as suggested by the literature, 43 out of 86 pharmaceuticals have been selected for a questionnaire survey for collecting data on their average consumption in inpatient department of multi speciality hospitals of bed strength 400 and above. The usage of these pharmaceuticals was confirmed from various stakeholders like doctors and pharmacists. But when the data of monthly consumption of these pharmaceuticals was collected from Central Procurement Agency, Government of Delhi and, it was found that out of these 43 pharmaceuticals, 19 are used most commonly and enormously. Other, than these 19 pharmaceuticals, 15 more pharmaceuticals belonging to antibiotics and cytotoxic class was found to be used in huge quantities. So, in total 34 pharmaceuticals are considered for prioritization.

IV. RESULT AND DISCUSSION

Development of priority list

The scaling weighing checklist method has been used to develop the priority list. All the pharmaceuticals have been given 1 point if it met the criterion and zero point for not satisfying the criterion. Each criterion has been given equal weightage. Points earned for 11 criteria have been added together. Depending upon their total points, the 34 pharmaceuticals have been classified into 3 categories, high priority (Class I); moderate priority (Class II) and Low priority pharmaceuticals (Class III). The pharmaceuticals having a cumulative total of 9 and above have been placed in high priority list. The pharmaceuticals satisfying 6-8 criteria are included in moderate priority list and those meeting 5 or less criteria are considered as low priority pharmaceuticals.

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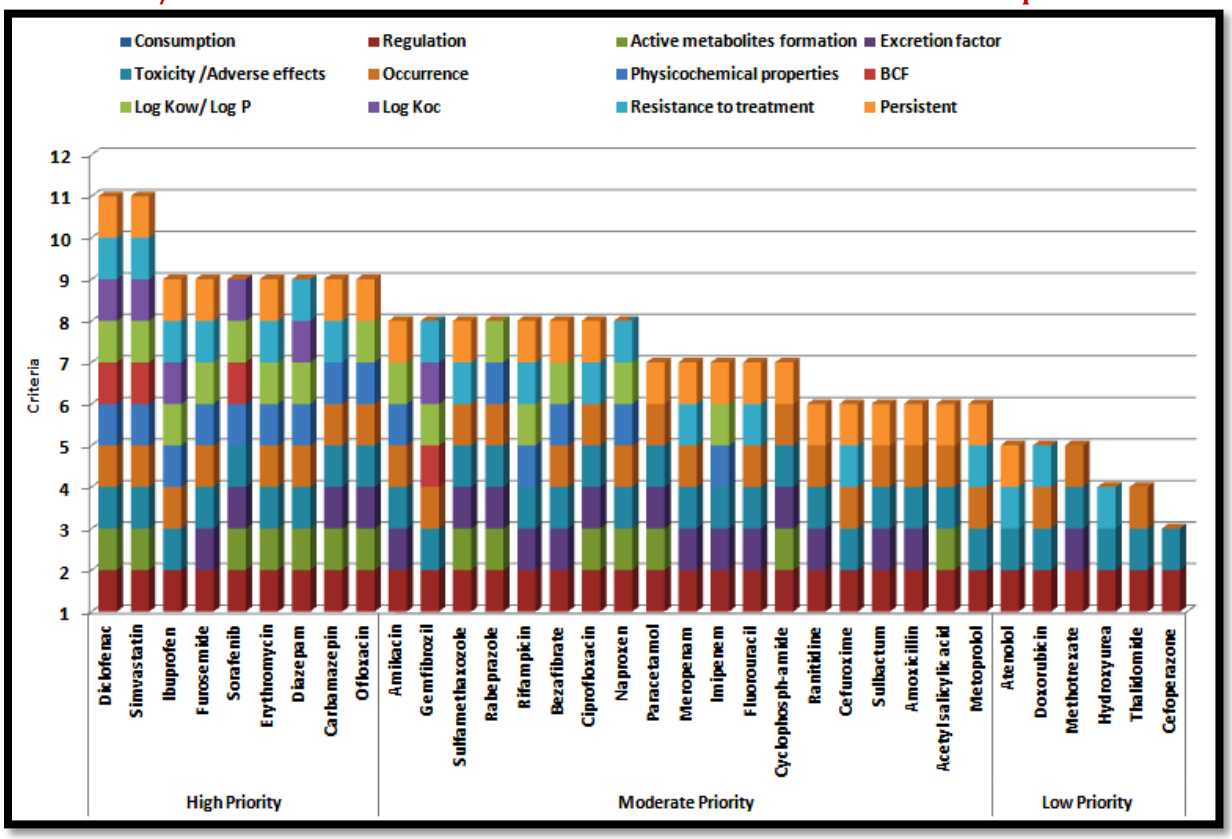

Graph 1: Prioritization on the basis of selection criteria

The high priority pharmaceuticals, moderate priority pharmaceuticals and low priority pharmaceuticals are listed below.

High priority list: Pharmaceuticals that are satisfying 9 or more criteria are classified as high priority pharmaceutical. There are 09 pharmaceuticals in this category that must be analyzed in the effluent before it is being discharged in the drain. All these pharmaceutical residues have been found to have maximum impact on aquatic ecology. These pharmaceuticals are considered as Class I. Following are the details of high priority pharmaceuticals:

1. **Consumption:** The list of 34 pharmaceuticals has been discussed with the experts in the field to know if they are used commonly. The high priority pharmaceuticals are among those selected by the experts. The annual consumption data has been fetched from Central Procurement Agency which provides pharmaceuticals to the hospitals belonging to Delhi Government. Also, a questionnaire survey was done in six multispecialty hospitals of Delhi. The sorafenib, diazepam and simvastatin pharmaceuticals are not used in huge quantities but they have high ecotoxicity and bio-accumulation potential. The major pharmaceutical consumption in Government hospitals of Delhi is shown in table no. 2. Apart, from this the Delhi Government hospitals also procure pharmaceuticals from vendors other than Central Procurement Agency which is not reflected in this table.

Table 2 Annual Consumption of high priority pharmaceuticals

Name of the pharmaceutical	Annual Consumption in Delhi Government Hospitals from March, 2016 to March, 2017 (in grams)
Diclofenac	3131868
Ibuprofen	6441402
Sorafenib	9038
Carbamazepin	1372020

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Diazepam	627
Ofloxacin	159176
Erythromycin	600262
Simvastatin	396
Furesmide	94074

Source: Office of Central Procurement Agency

2. **Regulation:** The chemicals/pharmaceuticals that are needed to be used judiciously are listed in international regulations. These pharmaceuticals should be made mandatory to be analyzed in the effluent generated at the source as well as water bodies. The detail about the high priority pharmaceuticals listed in various regulations is taken from CAS database accessed through Sci finder. (28)

Table 3 International regulations for high priority pharmaceuticals

Name of the pharmaceutical	Regulation
Diclofenac	Australian Inventory of Chemical Substances, European Union, REACH: List of Registered Substances, 2016, INSQ National Inventory of Chemical Substances in Mexico
Ibuprofen	INSQ National Inventory of Chemical Substances in Mexico, NZIoC New Zealand Inventory of Chemicals, 2006, PICCS Philippines Inventory of Chemicals and Chemical Substances, 2000, ECL Korean Government Gazette Notice, 2014, U.S. Environmental Protection Agency (EPA) Regulations - Toxic Substances Control Act (TSCA)
Sorafenib	REACH: List of Registered Substances, 2016
Carbamazepine	AICS Australian Inventory of Chemical Substances, June 1996 Ed, DSL Canada Gazette, Part II, February 11, 2004, IECSC Inventory of Existing Chemical Substances in China, 2013, REACH List of Pre-Registered Substances, March 2009, EINECS Annex to Official Journal of the European Communities, 15 June 1990, NZIoC New Zealand Inventory of Chemicals, 2006, PICCS Philippines Inventory of Chemicals and Chemical Substances, 2000, ECL Korean Government Gazette Notice, 2014, AREC Korean Government Gazette Notice, 2016, German Water Hazard Class Substances List, 09 Jan 2002.
Ofloxacin	REACH List of Pre-Registered Substances, March 2009, INSQ National Inventory of Chemical Substances in Mexico, 2012, ECL Korean Government Gazette Notice, 2014,
Erythromycin	AICS Australian Inventory of Chemical Substances, June 1996, DSL Supplement to Canada Gazette, Part I, January 26, 1991, IECSC Inventory of Existing Chemical Substances in China, 2013, REACH: List of Registered Substances, 2016, EINECS Annex to Official Journal of the European Communities, 15 June 1990, INSQ National Inventory of Chemical Substances in Mexico, 2012
Diazepam	AICS Australian Inventory of Chemical Substances, June 1996 , DSL Supplement to Canada Gazette, Part I, January 26, 1991, REACH List of Pre-Registered Substances, March 2009, EINECS Annex to Official Journal of the European Communities, 15 June 1990, ENCS Japanese Gazette. ENCS Designation: Japanese Pharmacopoeia (8th Ed.) substance, INSQ National Inventory of Chemical Substances in Mexico, 2012, NZIoC New Zealand Inventory of Chemicals, 2006.
Simvastatin	REACH List of Pre-Registered Substances, March 2009, INSQ National Inventory of Chemical Substances in Mexico, 2012, NZIoC New Zealand Inventory of Chemicals, 2006

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Furosemide	AICS Australian Inventory of Chemical Substances, June 1996, DSL Supplement to Canada Gazette, Part I, REACH List of Pre-Registered Substances, March 2009, INSQ National Inventory of Chemical Substances in Mexico, 2012, NZIoC New Zealand Inventory of Chemicals, 2006, PICCS Philippines Inventory of Chemicals and Chemical Substances, 2000.

Sorce: CAS database (28)

3. **Toxicity/ Ecotoxicity:** The toxicity assessment studies have been conducted by various researchers on these pharmaceuticals. The pharmaceutical residues are found to be toxic in fishes, daphnia and other aquatic organisms. Apart from this, few pharmaceutical residues are genotoxic, mutagenic and even teratogenic. (1)(5)(6)(7)(9)(11)(19)(20)(23)(24)(25)

4. **Occurrence in aquatic environment:** There is ample literature available on occurrence of these pharmaceuticals in different compartments of aquatic environment. The occurrence of pharmaceutical residues has been reported world widely. Although, the concentration of pharmaceutical residues has been reported in the range of mg/l to ng/l in wastewater and aquatic environment. (1)(4)(5)(6)(7)(9)(11)(19)(20)(21)(25)(26)

5. **Bio-concentration factor:** The BCF values at pH 1 to 10 have been taken from CAS database (28). The pharmaceuticals having BCF greater than 1000 can be considered as potentially bioaccumulable.

BCF value of <100 - not expected to bioaccumulate (Low potential)
BCF value of >100 but <1,000 - has the potential to bioaccumulate (Medium potential)
BCF value of >1,000 - has the potential to bioaccumulate significantly (High potential). (22)

The values of Bio-concentration factors are given in the table 4 below:

Table 4 Bio-concentration factors of High Priority Pharmaceuticals

Bio-concentration factors of High Priority Pharmaceuticals										
Name of the pharmaceutical	**pH-1**	**pH-2**	**pH-3**	**pH-4**	**pH-5**	**pH-6**	**pH-7**	**pH-8**	**pH-9**	**pH-10**
Diclofenac	1680	1670	1580	1010	220	25.2	2.82	1	1	1
Ibuprofen	270	269	260	195	55.4	6.83	1	1	1	1
Sorafenib	31	218	1240	2420	2670	2700	2700	2700	2680	2510
Carbamazepin	15.7	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2
Ofloxacin	1	1	1	1	1	1	1	1	1	1
Erythromycin	1	1	1	1	1	1	1.34	7.73	14.9	16.4
Diazepam	1.1	3.81	23.2	63.5	77.3	79	79.1	79.2	79.2	79.2
Simvastatin	2290	2290	2290	2290	2290	2290	2290	2290	2290	2290
Furosemide	32.8	30.2	16.7	3.09	1	1	1	1	1	1

Source: CAS Database (28)

This table determines the bio-accumulation potential of the high priority pharmaceuticals. The yellow color represents the low potential, green represents moderate potential and red shows high potential. The pH range in the natural environment generally ranges from 5-9. The diclofenac has moderate potential in this range however, it has a high potential in low pH range. The ibuprofen has a low potential in low pH range i.e acidic medium. The simvastatin and sorafenib have higher potential for bioaccumulation.

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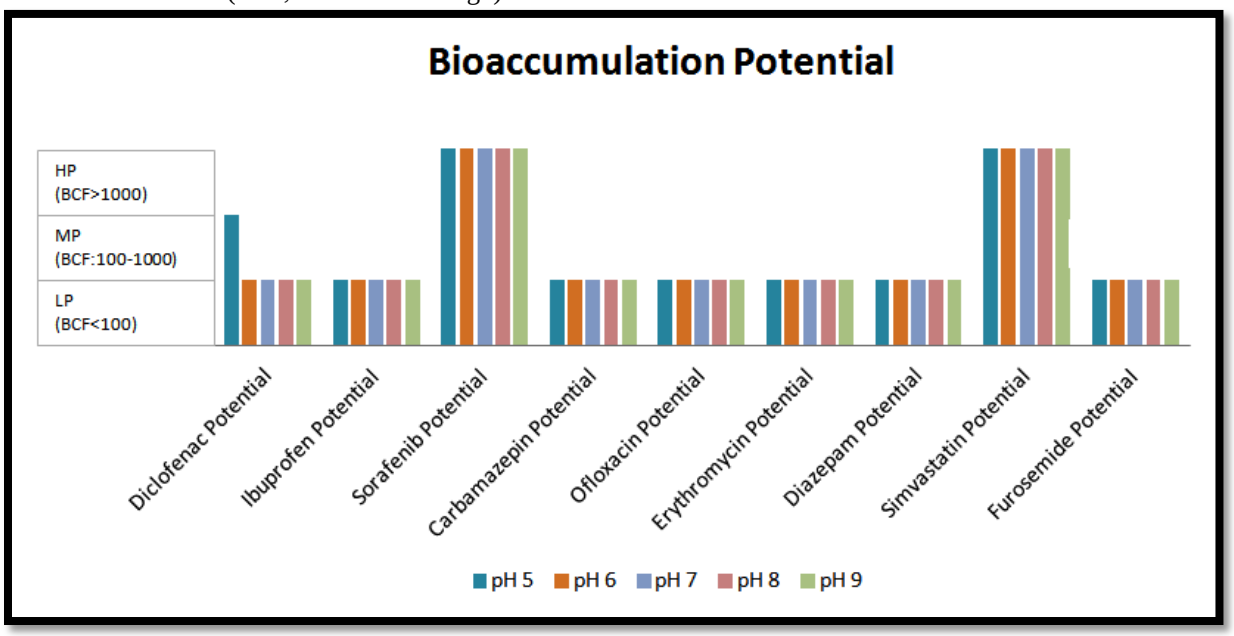
The graph 2 below depicts the pharmaceuticals belonging to categories of bio-accumulation potential in pH range of natural environment. (Low, Medium and High).



Graph 2 Bioaccumulation potential of the high priority pharmaceuticals

6. **Log Kow Values:** The octanol water partition coefficient decides the potential of adsorption as well as bioaccumulation. The Log Kow values of these pharmaceuticals has been taken from CAS Database (28).
   Log Kow < 2.5; Low potential for adsorption,
   4.0< Log Kow > 2.5 Moderate potential
   Log Kow > 4.0 High potential (20)(25)(26)

The pharmaceuticals having potential of adsorption as per their Log Kow values is depicted in the graph 3 below:

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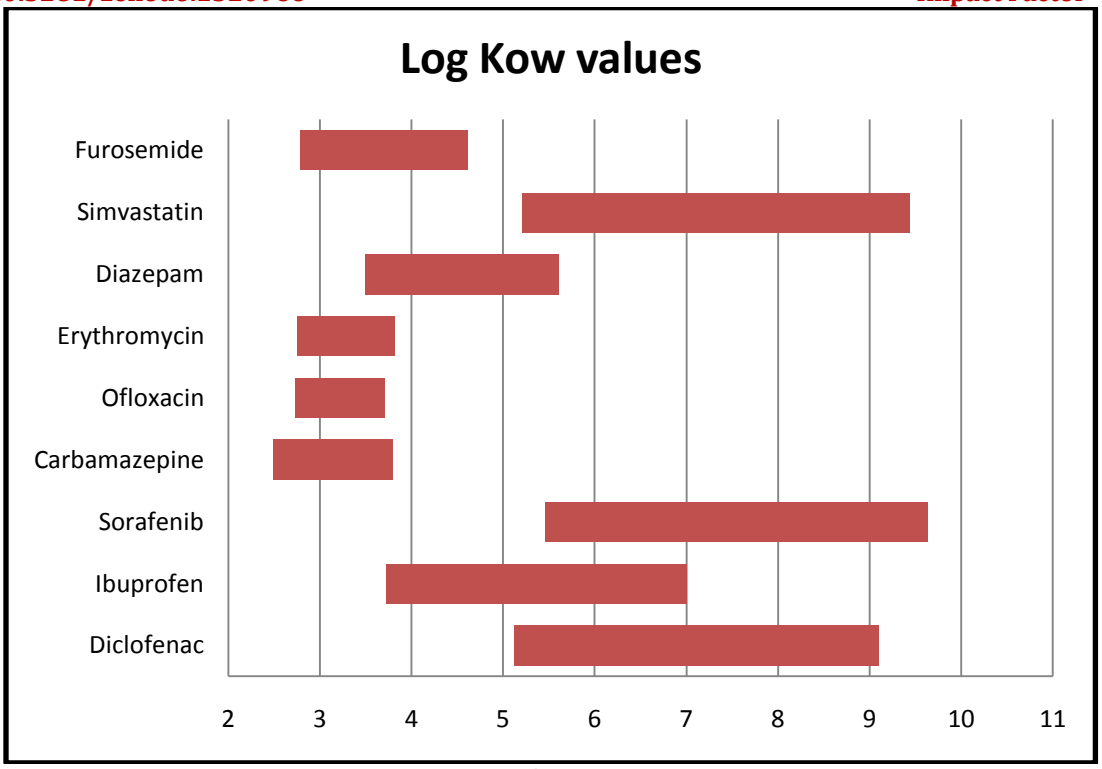
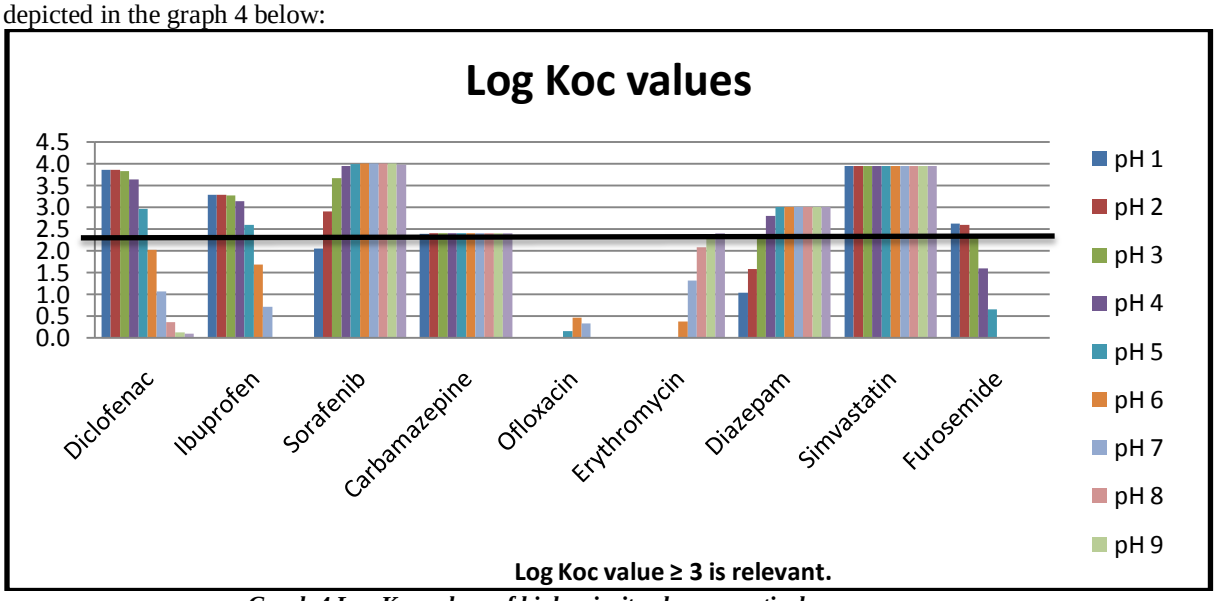


Graph 3 Log Kow values of high priority pharmaceuticals

7. **Log Koc Values:** A logKoc ≥ 3 is taken as a trigger value for sediment effect assessment. The pharmaceuticals having such values are persistent in sediment compartment. The Log Koc value of these pharmaceuticals has been taken from CAS Database (28). The pharmaceuticals having Log Koc ≥ 3 is depicted in the graph 4 below:



Graph 4 Log Koc values of high priority pharmaceuticals

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8. **Physico-chemical Properties:** These pharmaceuticals have such physico-chemical properties that make them relevant from the point of environment. The physico-chemical properties are depicted by Log Kow values, Log Koc values. The physico-chemical properties of the pharmaceutical determine the bioaccumulation potential, its persistence in the environment and its resistance to treatment.

9. **Active Metabolites:** The pharmaceuticals diclofenac, ibuprofen, sorafenib, erythromycin, diazepam, carbamazepine and ofloxacin forms active metabolites. The pharmaceuticals having active metabolites are given an extra weightage as the metabolites formed are also relevant from the point of view of environment.

Table 5 High priority pharmaceuticals having metabolites

Name of pharmaceutical	Metabolism
Diclofenac	This is a hydrophilic pharmaceutical forming metabolites like 4'-Hydroxydiclofenac, 3'-Hydroxydiclofenac, 5-Hydroxydiclofenac, 4′,5-dihydroxydiclofenac, Diclofenac acyl glucuronide. Two of these metabolites are biologically active, but to a much lesser extent than diclofenac.
Ibuprofen	It is a Lipophillic pharmaceutical and froms various metabolites such as Ibuprofen glucuronide, 2-Hydroxyibuprofen, 3-Hydroxyibuprofen,1-hydroxyibuprofen but these metabolites are not active.
Sorafenib	This pharmaceutical is lipophilic and forms eight pharmaceuticals including Pyridine N-oxide, Pyridine N-oxide glucuronide, Sorafenib beta-D-Glucuronide etc. Out of these Pyridine N-oxide is an active metabolite that is formed.
Erythromycin	It undergoes hepatic metabolism and less than 5% of the administered dose can be recovered in the active form in the urine. The metabolite ethylsuccinate is also formed.
Diazepam	The main active metabolite of diazepam is desmethyldiazepam. Diazepam and its metabolites are excreted mainly in the urine, predominantly as their glucuronide conjugates.
Carbamazepin	The carbamazepin forms metabolites. The carbamazepin-10, 11-epoxide is an active metabolite formed during the hepatic metabolism.
Ofloxacin	This forms metabolites like desmethyl and N-oxide ofloxacin.

Source : Goodman and Gilman's Manual of Pharmacology and Therapeutics (29)

Excretion factor: An excretion factor higher than 10% constitutes an additional risk. The frusemide, sorafenib, amikacin, carbamazepin and ofloxacin has relevant excretion factors.

Table 6 High priority pharmaceuticals having relevant excretion factor

Name of pharmaceutical	Excretion factor
Frusemide	About 90% excreted unchanged in urine.
Sorafenib	About 77% of the dose is excreted in faeces and 19% of the dose excreted in urine as glucuronidated metabolites.
Carbamazepin	The 72% of the dose is found in the urine while 28% in the faeces. Only 3% of the dose is recovered as unchanged carbamazepin.
Ofloxacin	The elimination is mainly by renal excretion. Almost 65%-80% of the dose is excreted 48 hours of dosing.

Source : Goodman and Gilman's Manual of Pharmacology and Therapeutics (29)

10. **Resistant to effluent treatment:** The literature survey has revealed that diclofenac, ibuprofen, amikacin, erythromycin, frusemide, simvastatin, carbamazepine, diazepam are resistant to conventional waswater

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treatment technologies. The pharmaceuticals resistant to effluent treatment are ought to get slowly decayed and will remain in the ecosystem for a longer period of time and thus impacts the ecosystem. (3)(4)(12)(15)

11. **Persistent:** The persistence of a pharmaceutical is guided by bioaccumulation potential, adsorption potential and other physico-chemical properties. The resistance to treatment also leads to the persistence of the pharmaceutical residue in the aquatic ecosystem. The literature survey has revealed that diclofenac, ibuprofen, amikacin, erythromycin, frusemide, simvastatin, carbamazepine, Ofloxacin are persistent in the aquatic environment. (25)(27)

Moderate Priority list: These are class II pharmaceuticals. There are 19 pharmaceuticals in this category. The pharmaceuticals in these category complied with 6 to 8 criteria. These are also relevant pharmaceuticals for analysis.
Low Priority List: There are 6 pharmaceuticals in this category which are relatively less relevant for different compartments of aquatic ecosystem. These pharmaceuticals meet 5 or less than 5 criteria.

V. CONCLUSION

The global occurrence of the pharmaceuticals and their residues in the water bodies strengthens the need to prioritize pharmaceutical residues for its treatment before disposal. The prioritization will enable regulating authorities to keep monitoring and check on the pharmaceutical residue concentration in the surface, ground and potable water.

The priority list has been made from limited set of selected pharmaceuticals through literature screening and consumption data of inpatient department of hospitals and Central Procurement Agency. The 12 important criteria have been considered in this study for identifying the priority pharmaceuticals. The criteria included in the study are consumption, toxicity/ ecotoxicity, occurrence in surface water, bioaccumulation potential and other important physicochemical properties. In this study, equal weightage has been given to all the criteria for selection, if certain criteria is considered to have more or less weightage, it might lead to minor changes between the list, however, these lists are capable enough of giving an insight into the relevant pharmaceuticals and relevance of analyzing these pharmaceutical residues to assess the quality of wastewater discharged. These criteria will remain same locally as well as globally, however, pharmaceuticals relevant for study may vary depending upon their consumption.

The high priority list has been developed including 9 pharmaceuticals being most commonly consumed in hospitals of Delhi. The high priority pharmaceuticals belongs to various classes including non-steroidal anti-inflammatory pharmaceuticals like diclofenac, ibuprofen; antibiotics like ofloxacin and erythromycin; antiepileptic pharmaceutical that is carbamazepine; antidepressant like diazepam, lipid regulator like simvastatin and furosemide which is a diuretic. This list of pharmaceuticals represent minimum that should be considered while assessing the quality of hospital effluent being discharged into drain which is thus leading to water bodies and thereby affect its quality. The most commonly consumed pharmaceuticals have been incorporated, so there is possibility that other important pharmaceuticals might have not been incorporated due to constraints in collecting consumption data. Also, the literature on occurrence of various pharmaceuticals belonging to different therapeutic classes is limited. There are three lists that have been developed high priority, moderate priority and low priority list of pharmaceuticals. With respect to its impact on aquatic environment, this paper would develop a protocol for selection of priority pharmaceuticals. The approach for selecting high priority pharmaceuticals provides an efficient and practical base to manage the risks related to discharge of pharmaceuticals in water bodies. This paper would help regulating agency to consider setting standards for important pharmaceutical residues in wastewater discharged from hospitals, veterinary, animal farms, pharmaceutical industries and other major sources of pharmaceutical consumption.

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